

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Nicholas Valiante, Jr.
Title: USE OF TRYPTANTHRIN
COMPOUNDS FOR IMMUNE
POTENTIATION
Appl. No.: 10/762,873
Filing Date: 1/21/2004
Examiner: Yong Soo Chong
Art Unit: 1617
Confirmation Number: 5927

DECLARATION OF NICHOLAS VALIANTE, JR.

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Nicholas Valiante, Jr., hereby declare that:

I. I received a Ph.D. in Immunology from the University of Pennsylvania (1994). For the last 19 years I have worked on the innate immune response, cytokine networks and inflammation including 3.5 years as a research fellow at Stanford University and 10 years in the vaccine industry. I have published >60 scientific papers and I am regular consultant for the NIH, FDA, CDC and US Dept. of Defense. In my 10 years in vaccines research I have served as the Project leader of the vaccine adjuvant platform for 5 years. I am currently Research Director for Novartis Vaccines and the Project Leader of a Novartis-wide platform on immune potentiator discovery.

2. I am the inventor of the subject matter described and claimed in U.S. Patent Application Serial No. 10/762,873.

3. I thank Examiner Chong for allowing Mr. Hugo Eng and Ms. Lorna Tanner to discuss the outstanding rejections in this application. I understand that a declaration, which I am now providing, regarding the properties of the tryptanthrin compounds would be helpful in advancing the prosecution of this application.

4. I understand that the Office has rejected the present claims as being obvious in view of US 5,441,955 to Baker. Baker teaches that certain tryptanthrin compounds directly inhibit growth of the tuberculosis bacteria through physical contact with the bacteria. Baker discloses an assay wherein cultures of various strains of *M. tuberculosis* are grown and then treated with the tryptanthrin compounds. The assay clearly indicates that inhibition of tuberculosis bacteria is direct and does not involve the recruitment of molecular components of the immune system, as such components are not present in the assay. Thus Baker does not teach use of the tryptanthrin compounds as immune potentiators or as adjuvants.

5. The present application has shown surprisingly that tryptanthrin compounds can be effective in generating an immune response. Table 1 (right-most column) of the present application shows the ability of the compounds to elicit production of the cytokine TNF- α . The ability of the tryptanthrins to stimulate TNF- α production is unexpected based on the previously known properties of the compounds. The disclosed findings therefore indicate that the tryptanthrin compounds have utility as immune potentiators.

6. Immune potentiators, including Toll-like Receptor agonists, induce cytokines such as TNF- α *in vitro* and compounds that induce these cytokines have been shown to be adjuvant candidates *in vivo* when tested. Therefore, that tryptanthrins induce TNF- α from immune cells *in vitro* renders them adjuvant candidates *in vivo*.

7. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that false statements and the like made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the patent.

Date

10/31/07

A handwritten signature in dark ink, appearing to read 'Nicholas Valiante, Jr.', written over a horizontal line.

Nicholas Valiante, Jr.